

CLAIMS

What is claimed is:

1. A method for directly identifying a non-endogenous compound as a compound
5 having an activity selected from the group consisting of: inverse agonists, parallel agonists, and partial agonists, to a non-endogenous, constitutively activated version of known G protein-coupled receptor, said receptor comprising a transmembrane-6 region and an intracellular region, comprising the steps of:

- (a) selecting a non-endogenous version of a known GPCR having an amino
10 acid sequence selected from the group consisting of SEQ.ID.NO.:425;
SEQ.ID.NO.:427; SEQ.ID.NO.:429; SEQ.ID.NO.:431;
SEQ.ID.NO.:433; SEQ.ID.NO.:435; SEQ.ID.NO.:437;
SEQ.ID.NO.:439; SEQ.ID.NO.:441; SEQ.ID.NO.:443;
SEQ.ID.NO.:445; SEQ.ID.NO.:447; SEQ.ID.NO.:449;
15 SEQ.ID.NO.:451; SEQ.ID.NO.:453; SEQ.ID.NO.:455;
SEQ.ID.NO.:457; SEQ.ID.NO.:459; SEQ.ID.NO.:461;
SEQ.ID.NO.:463; SEQ.ID.NO.:465; SEQ.ID.NO.:467;
SEQ.ID.NO.:469; SEQ.ID.NO.:471; SEQ.ID.NO.:473;
SEQ.ID.NO.:475; SEQ.ID.NO.:477; SEQ.ID.NO.:479;
20 SEQ.ID.NO.:481; SEQ.ID.NO.:483; SEQ.ID.NO.:485;
SEQ.ID.NO.:487; SEQ.ID.NO.:489; SEQ.ID.NO.:491;
SEQ.ID.NO.:493; SEQ.ID.NO.:495; SEQ.ID.NO.:497;
SEQ.ID.NO.:499; SEQ.ID.NO.:501; SEQ.ID.NO.:503;
SEQ.ID.NO.:505; SEQ.ID.NO.:507; SEQ.ID.NO.:347;

SEQ.ID.NO.:509; SEQ.ID.NO.:351; SEQ.ID.NO.:355;
 SEQ.ID.NO.:359; SEQ.ID.NO.:363; SEQ.ID.NO.:367;
 SEQ.ID.NO.:371; SEQ.ID.NO.:375; SEQ.ID.NO.:379;
 SEQ.ID.NO.:383; SEQ.ID.NO.:387; SEQ.ID.NO.:391;
 SEQ.ID.NO.:511; SEQ.ID.NO.:513; SEQ.ID.NO.:515;
 SEQ.ID.NO.:517; SEQ.ID.NO.:519; SEQ.ID.NO.:521;
 SEQ.ID.NO.:523; SEQ.ID.NO.:525; SEQ.ID.NO.:527;
 SEQ.ID.NO.:529; SEQ.ID.NO.:531; SEQ.ID.NO.:533;
 SEQ.ID.NO.:535; SEQ.ID.NO.:537; SEQ.ID.NO.:539;
 SEQ.ID.NO.:541; SEQ.ID.NO.:543; SEQ.ID.NO.:545;
 SEQ.ID.NO.:547; SEQ.ID.NO.:549; SEQ.ID.NO.:551;
 SEQ.ID.NO.:553; SEQ.ID.NO.:555; SEQ.ID.NO.:557;
 SEQ.ID.NO.:559; SEQ.ID.NO.:561; SEQ.ID.NO.:563;
 SEQ.ID.NO.:565; SEQ.ID.NO.:567; SEQ.ID.NO.:569;
 SEQ.ID.NO.:571; SEQ.ID.NO.:573; SEQ.ID.NO.:575;
 SEQ.ID.NO.:577; SEQ.ID.NO.:395; SEQ.ID.NO.:399;
 SEQ.ID.NO.:403; SEQ.ID.NO.:407; SEQ.ID.NO.:411;
 SEQ.ID.NO.:415; SEQ.ID.NO.:419; SEQ.ID.NO.:423;
 SEQ.ID.NO.:579; and SEQ.ID.NO.:581;

5

10

15

20

- (b) confirming that the selected non-endogenous GPCR of step (a) is constitutively active;
- (c) contacting a non-endogenous candidate compound with the non-endogenous, constitutively activated GPCR of step of (b); and

(d) determining, by measurement of the compound efficacy at said contacted receptor, whether said non-endogenous compound having inverse agonist activity as an inverse agonist or agonist activity is an agonist to said receptor of step (b).

2. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:425.
3. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:427
4. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:429.
5. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:431.
6. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:433.
7. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:435.
8. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:437.
9. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:439.
10. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:441.
11. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:443.

12. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:445.
13. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:447.
- 5 14. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:449.
15. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:451.
- 10 16. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:453.
17. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:455.
18. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:457.
- 15 19. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:459.
20. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:461.
- 20 21. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:463.
22. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:465.
23. The method of claim 1 wherein the non-endogenous GPCR of 467.



24. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:469.
25. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:471.
- 5 26. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:473.
27. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:475.
28. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:477.
- 10 29. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:479.
30. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:481.
- 15 31. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:483.
32. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:485.
33. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:487.
- 20 34. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:489.
35. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:491.

36. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:493.
37. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:495.
- 5 38. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:497.
39. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:499.
- 10 40. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:501.
41. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:503.
42. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:505.
- 15 43. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:507.
44. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:347.
- 20 45. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:509.
46. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:351.
47. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:355.

48. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:359.
49. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:361.
50. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:367.
51. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:371.
52. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:375.
53. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:379.
54. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:383.
55. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:387.
56. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:391.
57. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:511.
58. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:513.
59. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:515.

60. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:517.
61. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:519.
- 5 62. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:521.
63. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:523.
64. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:525.
- 10 65. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:527.
66. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:529.
- 15 67. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:531.
68. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:533.
69. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:535.
- 20 70. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:537.
71. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:539.

72. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:541.
73. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:543.
- 5 74. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:545.
75. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:547.
76. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:549.
- 10 77. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:551.
78. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:553.
- 15 79. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:555.
80. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:557.
81. The method of claim 1 wherein the non-endogenous GPCR of step b is step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:559.
- 20 82. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:561.
83. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:563.

84. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:565.
85. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:567.
- 5 86. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:569.
87. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:571.
88. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:573.
- 10 89. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:575.
90. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:577.
- 15 91. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:395.
92. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:399.
93. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:403.
- 20 94. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:407.
95. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:411.

96. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:415.

97. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:419.

5 98. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:423.

99. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:579.

10 100. The method of claim 1 wherein the non-endogenous GPCR of step (b) is an amino acid sequence having the sequence of SEQ.ID.NO.:581.

101. The method of claim 1 further comprising the following step:

assessing, by using an endogenous ligand based assay, the impact of the non-endogenous compound of step (d) on the binding of an endogenous ligand for the known GPCR version of the non-endogenous version of said known GPCR of step (a) with said known GPCR.

15

102. The method of claim 101 wherein said non-endogenous compound is an allosteric modulator of said known GPCR.